

EBPG Guideline on Nutrition

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Guideline 1. Prevalence of malnutrition and outcome

- Nutritional status should be assessed at the start of haemodialysis (Opinion).
- Protein–energy malnutrition should be avoided in maintenance haemodialysis because of poor patient outcome (Evidence III).
- In absence of malnutrition, nutritional status should be monitored every 6 months in patients <50 years of age (Opinion).
- In patients >50 years of age, and patients undergoing maintenance dialysis for more than 5 years, nutritional status should be monitored every 3 months (Opinion).

Rationale

Malnutrition is considered to be one of the late complications of chronic renal failure. A sub-analysis of the Modification of Diet in Renal Disease (MDRD) study, however, demonstrated that progressive renal insufficiency was associated with a spontaneous decline in protein intake. Predialysis patients appeared to have a spontaneous protein intake of <0.7 g/kg/day [1], which is below the minimal recommended daily intake. Thus, malnutrition in haemodialysis patients may already originate during stage IV of chronic renal failure.

It has been demonstrated that serum albumin and creatinine increase during the first half year of haemodialysis [2,3], suggesting an improvement of

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nutritional status after the initiation of dialysis. Nevertheless, many studies have reported on the presence of malnutrition in a large number of dialysis patients [4–7]. In the French national cooperative study [6], that included 7123 patients, nutritional status was determined by body mass index (BMI), normalized protein catabolic rate (nPCR) and several laboratory values. Life-threatening malnutrition was present in up to 36% of the patients. Low protein intake and low dialysis efficacy were associated with the presence of malnutrition. Several other studies demonstrated that haemodialysis patients eat less protein and fewer calories than prescribed, which is associated with a higher rate of malnutrition [4,5,7].

Several small and large scale cohort studies have revealed that protein–energy malnutrition is associated with increased morbidity, mortality and impaired quality of life [8–19]. Herselman *et al.* [10] demonstrated an association between a composite score for protein–energy malnutrition and infection-related morbidity in a group of haemodialysis patients. A recent paper demonstrated that in patients with an appropriate dialysis efficacy ($Kt/V \geq 1.2$) low serum albumin and low protein intake, measured as low nPCR, were associated with a higher risk of hospitalization and mortality [17]. Data from the United States Renal Data System (USRDS) database [13] as well as data from the large Dialysis Outcomes and Practice Patterns Study (DOPPS) cohort [14] confirm that malnourished dialysis patients have an increased risk of mortality. In the USRDS DMMS-1 cohort analysis protein–energy malnutrition was established through serum albumin levels, BMI and notification by the treating physicians in the patient medical files of the existence of malnutrition [13]. From this data set of 5058 patients it was concluded that patients who were considered malnourished by their physicians, had a 27% greater risk of cardiovascular death. In addition it was shown that for each one-unit decrease in BMI the risk for cardiovascular death rose by 6% and each 1 g/dl fall in serum albumin level was associated with a 39% increase in risk of cardiovascular death. A recent study reported that both malnutrition, established by measurement of total body nitrogen by *in vivo* neutron activation analysis, and serum albumin were independent predictors of mortality in incident haemodialysis patients [19]. Hypoalbuminaemia appeared also to be a predictor of vascular morbidity. In DOPPS, a prospective observational study, nutritional status is investigated by means of a modified subjective global assessment (mSGA), BMI, serum albumin and some other laboratory parameters at baseline ($n = 7719$) and after 6 months ($n = 3739$; [14]). Patients with severe malnutrition according to mSGA had a 33% higher mortality risk and patients with moderate malnutrition a 5% increased risk. In patients with the lowest BMI quartile the mortality risk was 60% higher than that of patients in the highest quartile. In addition it was demonstrated that patients who had a loss in BMI

of $\geq 3.5\%$ had an increase in mortality risk. Likewise, both a low serum albumin level as well as a fall in serum albumin was strongly associated with an elevated mortality risk.

Apart from the elevated risk of mortality, results from the HEMO study have revealed that malnutrition, established with anthropometric measurements, serum albumin and PCR, was associated with impaired physical functioning [20] and impaired quality of life [12]. Likewise, Koo *et al.* [18] reported an association between depression and malnutrition in a group of chronic haemodialysis patients.

It is widely appreciated that age negatively affects outcome of dialysis patients. It has been demonstrated only in a few studies that malnutrition contributes to the increased mortality risk of older dialysis patients [21,22]. In the HEMO study, it was demonstrated that middle age (> 50 years) and older (> 65 years) dialysis patients had lower dietary energy and protein intake, serum albumin levels and nPCR compared with young dialysis patients (< 50 years) despite similar dialysis efficacy measured as equilibrated Kt/V (eKT/V) [21]. Such indications for malnutrition in the older patients were associated with higher morbidity. In a French cohort study, it was shown that in dialysis patients over 75 years, malnutrition negatively affected overall survival despite adequate dialysis treatment [22].

In several small and larger studies dialysis vintage appeared to have a clear negative effect on nutritional status of dialysis patients [16,23–29]. In a cohort study of 3009 patients, Chertow *et al.* [27] were able to demonstrate that dialysis vintage was associated with a decline in nutritional parameters and that every year on dialysis was associated with a 6% increase in the risk of dying. Likewise, in the HEMO study it was shown that patients over 5 years on dialysis had significantly lower anthropometric parameters suggesting an impaired nutritional status compared with patients shorter on dialysis [16]. This was also shown in studies with more sophisticated tools for determination of nutritional status [24,29].

Thus an adequate monitoring of nutritional status is an important step of haemodialysis patients care and allows for the identification of body composition alterations associated with increased morbidity and mortality.

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Guideline 2. Diagnosis and monitoring of malnutrition

Protein–energy malnutrition and wasting are strong predictors of death among haemodialysis patients. There is not a single measurement that provides complete and unambiguous assessment of the nutritional status of haemodialysis patients (see below Guideline 2.1). Ideally, a nutritional marker should not only predict outcome, but it should also be an inexpensive, reproducible and easily performed test that is not affected by such factors as inflammation, gender, age and systemic diseases. No such ideal nutritional marker is available at present. Thus the use of a panel of anthropometric and biochemical measurements that correlate with nutritional status is required to assess protein–energy malnutrition in a given individual.

Guideline 2.1. Diagnosis of malnutrition

- Malnutrition should be diagnosed by a number of assessment tools including (Opinion):
 - (A) Dietary assessment
 - (B) Body mass index
 - (C) Subjective global assessment (SGA)
 - (D) Anthropometry
 - (E) nPNA
 - (F) Serum albumin and serum prealbumin
 - (G) Serum cholesterol
 - (H) Technical investigations (bioimpedance-metry, dual X-ray absorptiometry, near-infrared reactance)

(A) Dietary assessment

- Every haemodialysis patient should have access to a qualified dietitian (Opinion).
- All haemodialysis patients should receive a care plan and individualized dietary information in writing. Both the care plan and dietary information should be reviewed frequently depending on individual medical conditions and personal circumstances (Opinion).
- All haemodialysis patients should be reassessed and counselled within 1 month after haemodialysis has started (Opinion).
- Malnourished haemodialysis patients should be reassessed and counselled more frequently (Opinion).

Rationale

Dietitians are qualified professionals and experts in the application of science in nutrition and metabolism. Training includes interview and counselling techniques. They enable patients to adapt their regular diet to a diet that includes individual requirements for maintenance haemodialysis (MHD), based on personal circumstances while also recommending nutritional support as and when needed. Most but not all patients will have received nutritional assessments and counselling prior to starting MHD. It is most important to adjust their diet as soon as possible, preferably within 1 month. All dietary information provided should be in writing and details should be recorded in the patient's care plan. It is essential to evaluate and modify individual dietary regimens after a further month or sooner as needed. Stable MHD patients should be interviewed every 3 or 6 months according to age (<50 years, every 6 months, >50 years every 3 months, see Guideline 1), and dialysis vintage (<5 years, every 6 months, >5 years every 3 months, see Guideline 1) as indicated to improve dietary compliance [1,2]. Hospitalized patients and patients requiring naso-gastric tube feeding or intra-dialytic parenteral nutrition (IDPN) should be assessed within 2–3 days and require follow-up at least once weekly for 2 weeks or until stable. Thereafter follow-up and monitoring can be extended to once per month or as required [1].

Assessment of dietary intake can be obtained by dietary records and/or food questionnaires:

Dietary records. Existing methods to record food intake of individual patients range from 24-h-recall to 3 and 7 days diet diaries, the expertise of a qualified dietitian is essential to complete and calculate these accurately. Dietary assessments are essential as there are no alternatives to calculate nutrient intake, now using special computerized food composition programmes and they are part of a set of methods assessing the overall nutritional status of patients

on MHD. Data obtained from unsupervised food recordings and covering a short period of time should be interpreted with caution as results can be subjective and incomplete. Patients may overestimate when their intake is poor or underestimate when their intake is good. Also perceptions of portion sizes differ resulting in inaccurate food assessments [3]. The latter can be overcome by using commercial replica food models or a photographic food atlas [4].

Twenty-four hour dietary recall: Recalling what a patient consumed as food and drink during the previous 24 h is a simple method that requires a minimum of professional input and may be used in the routine follow-up in nutritionally stable patients when there are constraints on dietetic input [2]. It can reveal major imbalances or obvious dietary inadequacies or highlight areas of concern which need further investigation. It is a good starting point for more detailed discussions and counselling. The 24-h recall interview technique depends on memory and patients may underestimate actual intake. Recalling food intake even during the previous 24 h may be difficult for the elderly suffering from memory impairment. Intake is confined to a short period and may not represent a typical food intake reflecting daily variations. Longer recall periods may provide inaccurate information as patients become less motivated and several shorter periods of 2–3 days may provide more accurate information to assess protein and energy intake.

Three days food records: In patients with a stable food intake a period of <7 days may be adequate to assess protein and energy intake. The Kidney Disease Outcomes Quality Initiative (K/DOQI) Recommendations for Nutritional Management [2] suggest a 3-day diary which includes a dialysis day, a weekend day and a non-dialysis day. This provides a closer insight into dietary habits. A 3-day diary is preferred as patients do not always comply with accurate recordings for a longer period due to lack of motivation. Patients should be taught how to complete diaries using household measures and food models if available. A dietary record must include the day and time when meals, snacks and beverages are taken, a description of the food or drink, methods of food preparations, missed meals, amount consumed in restaurants and the amount of consumed convenience and processed foods.

Seven days food records or diet diaries: A minimum of 7 days is required to assess protein and energy intake to stay within 10% of SE, but may not be adequate to assess nutrient intake when these are obtained from few foods, such as Vitamin C, as 36 days are required to obtain the same accuracy [4]. The advantage of a 7-day diary is that variations in food intake over a longer period are included. In order to accurately calculate protein catabolic rate (PCR), dietary protein intake (DPI) and dietary energy intake (DEI), Kloppenburg *et al.* [5] found that a 7-day period correlated better with the mean of three consecutive PCR measurements and average protein and energy

intake compared with a single measurement during the same period. Dietary protein and energy intake vary considerably from day to day as a result of dialysis treatment sessions and associated disturbances in food intake. In this study, qualified dietitians instructed patients regarding accurate recording techniques using standard household measures to record day to day food intake. Patients were also contacted when their records needed further discussion.

Appetite assessment

A specially designed questionnaire can be helpful in addition to food diaries to calculate nutrient intake in a large number of patients during a longer period. In the recent HEMO Study patients (1901 at onset) completed dietary records during an assigned 2-day period (including a dialysis day) after receiving detailed instructions from specially trained dietitians. The follow-up period lasted 7 years [6]. Self assessed appetite was evaluated with the Appetite and Diet Assessment Tool (ADAT) to monitor changes in appetite and dietary habits on both dialysis and non-dialysis days. Other dietary information affecting nutritional intake was also obtained. Further research is required to assess prospectively the predictive power of the ADAT in its ability to monitor and detect changes in dietary habits and appetite [6]. In another study an Appetite and Dietary Assessment Questionnaire (ADAQ) was developed by Lou *et al.* [7] to predict inadequate intake in a small number of patients (44) on chronic HD (CHD). Diet-diary assisted recalls (DDAR) were used to evaluate nutritional intake. Dialysis and non-dialysis day's diet data and PCR differences were also studied. The relationship between ADAQ and protein-energy intakes calculated by DDAR was highly significant. The questionnaire was found to be simple and could be used as a screening tool to detect poor nutrition and correct factors that could lead to malnutrition.

(B) Body mass index (BMI)

- Haemodialysis patients should maintain a BMI >23.0 (Evidence level III)

Rationale

BMI is known to predict the clinical outcome of disease. BMI is dependent on muscle and fat mass and total body water content, however weight changes over a period of time can still be of clinical value and more so in the case of unplanned weight loss over a short period of time. When assessing BMI it should be remembered that a higher percentage of muscle mass is seen in young people, athletes and body builders and a higher percentage of fat mass in less mobile and elderly patients.

Several studies have shown that a BMI of 23 and higher reduces the risk of morbidity and

mortality [8–12]. BMI and anthropometric measurements change with age and dialysis vintage in diabetic and non-diabetic patients [13–15]. In a retrospective analysis, Kopple *et al.* [8] investigated the relationship between BMI and the rate of mortality in 12 965 MHD patients. BMI was calculated using post-dialysis weight and the mean age of patients was 60.3 years. The National Health and Nutrition Evaluation Survey (NHANES) II data, representing men and women with normal weights, were compared with weights of MHD patients matching in height, gender and were divided in two age ranges, 25–54 and 55–74 years. The results showed that death rates in MHD patients with a BMI in the 10th, the 10–25th and 25–50th percentile were significantly higher compared with men with a BMI in the 50th percentile or higher. Women show a similar improvement in death rates with increasing BMI. This study also showed that advancing age was strongly associated with odds of death with lower BMI. Thus BMI is a strong predictor of mortality in MHD patients over a 12-month period and that is an independent predictor of increasing mortality rates in patients below the 50th percentile. The 50th percentile corresponds with a BMI of at 23.6 for males and 24.3 for women (see Appendix) [1].

Data from a cohort of 1610 patients of the French Study Group Nutrition in Dialysis indicated that nutritionally stable and well-dialysed MHD patients with a BMI of 23.0 ± 4.5 and albumin concentrations within normal range had an increased survival rate of $89.7 \pm 0.8\%$ at 1 year and $78.4 \pm 1.2\%$ at 2 years [13,15]. From the Case Mix Adequacy Special Study of the USRDS with a national sample of 3607 MHD patients with a mean age of 58.8 years, Leavey *et al.* [10] concluded that BMI at baseline was a valuable independent predictor of mortality risk and persisted 5 years later. The prospective DOPPS provided baseline demographic, comorbidity and BMI data on 9.714 MHD patients in USA and Europe during 1996–2000 [11]. Multivariate survival analysis was used to evaluate the relationship between BMI and relative risk (RR) of mortality in MHD patients subdivided by continent, race, gender, tertiles of severity in illness (based on a score derived from comorbid conditions and serum albumin levels), age ranges (<45, 46–64 and >65 years), smoking and diabetic status. Results showed a lowering in the RR of mortality as BMI increased and this was statistically relevant but not for patients in the younger age group of <45 years who were also in the healthiest tertile of comorbidity. A BMI of <20 was consistently associated with the highest mortality risk [11,12]. Abbott *et al.* [12] also concluded that a higher BMI was associated with improved survival in 1675 cohort patients on MHD with a follow-up of 5 years, in a retrospective study of the USRDS Dialysis, Morbidity and Mortality Wave II Study (DMMS). Results showed that patients with a high BMI $\geq 30 \text{ kg/m}^2$ had a 5-year survival of 39.8% vs 32.3% for patients with a lower BMI and this was statistically significant ($P = 0.001$).

(C) Subjective global assessment (SGA)

- SGA should be used to identify severe malnutrition in haemodialysis patients (Evidence level III).

Rationale

SGA is based on a combination of subjective and objective features from the medical history and physical examination. A modified version of the SGA has been used in the Canada/United States Peritoneal Dialysis Study (CANUSA) and DOPPS studies (see Appendix). It was demonstrated that lower values of the mSGA were associated with a higher mortality risk [16]. The investigators concluded that in haemodialysis patients malnutrition, as indicated by low values obtained with the mSGA, was associated with higher mortality risk [16]. In a prospective observational study, it was also shown that patients with the lowest SGA score had higher mortality and hospitalization rates [17]. In a direct comparison with the determination of body nitrogen content by means of *in vivo* neutron activation analysis it was demonstrated that SGA was able to differentiate severely malnourished patients from those with normal nutrition, but appeared not to be a reliable predictor of the degree of malnutrition [18].

(D) Anthropometry

- Anthropometry in MHD patients should be assessed immediately after dialysis (Opinion).
- Anthropometry (Mid Arm Circumference (MAC), Mid-Arm Muscle Circumference (MAMC) and four site Skin Fold Thickness (SFT) should be performed by the same individual on the non-fistula arm (Opinion).

Rationale

BMI, Four-site skin fold thickness (SFT), mid-arm-circumference (MAC) and mid-arm-muscle-circumference (MAMC) are anthropometric screening methods to assess fat and lean body mass and may detect a potential risk for Protein and Energy Wasting (PEW). These are easy to use, widely available and cost effective tools to help assess nutritional status of patients on MHD but fluid status influences calculations.

Four-site SFT, MAC and MAMC: these anthropometric measurements are important for overall nutritional assessment. Measuring muscle mass, MAC and MAMC, is essential to assess muscle mass. It is necessary to perform skin fold thickness at four sites to obtain an accurate assessment of total body fat: triceps, biceps, sub-scapular and ileac crest. The Frisancho Tables (1984) and Durnin and Womersley (1974) equations are used to calculate lean body mass and body fat percentage from obtained details (see Appendix for methods).

Comparing SFT and bio impedance analysis (BIA): Oe *et al.* [19] evaluated body composition [lean body mass (LBM), body fat (BF) and total body water (TBW)] using SFT and BIA techniques in 20 stable MHD patients pre- and post-dialysis. These authors showed a good agreement between the two techniques ($R=0.93$, $P < 0.005$) and proposed that BIA might be the preferred method, as BIA is not operator dependent and requires minimal training to assess fluid status. Kamimura *et al.* [20] also found that SFT measurements were comparable with BIA and remain interesting for routine body fat assessment. Ninety clinically stable MHD patients were studied; body fat measurements using SFT and BIA were similar (13.5 ± 6.2 kg and 13.7 ± 6.7 kg). Further research is recommended to obtain references for body composition assessment that are simple to use in the routine care of MHD patients.

(E) Normalized protein nitrogen appearance (nPNA)

- Normalized PNA should be measured in clinically stable haemodialysis patients and be above 1.0 g/kg ideal BW/day (Evidence level III) (see Guideline 3).

Rationale

Normalized PNA provides an independent and less time consuming assessment of dietary protein intake. Nitrogen balance, the difference between intake and losses, is zero in the steady state or slightly positive. Both net protein breakdown under fasting conditions and dietary protein requirements are strongly influenced by body mass. In order to normalize PNA it should be related to body weight of the patient. When determining nPNA, patients should be stable and neither anabolic nor catabolic [21]. The protein equivalent of total PNA can be estimated from interdialytic changes in urea nitrogen concentrations in serum and urine (see Appendix). A recent study in more than 50,000 US adult haemodialysis patients reported that mortality was lowest for patients having a nPNA between 1.0 and 1.4 g protein/kg BW/day; furthermore, when patients had a decreased nPNA after a 6-month follow-up, the 18-month subsequent mortality increased [22]. PNA should however not be used alone to evaluate nutritional status, but rather as one of several independent measures when evaluating nutritional status.

(F) Serum albumin and serum prealbumin

- Serum albumin should be above 40 g/l by bromocresol green method (Evidence level III).
- For other albumin assessment methods the target values should be adapted to the above (Opinion).
- Serum prealbumin should be above 0.3 g/l (Evidence level III)